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TITLE: A Multidisciplinary Intervention for Encopresis in Children with ASD

PRINCIPAL INVESTIGATOR: Nathan Call, PhD, BCBA-D

CONTRACTING ORGANIZATION: Emory University
Atlanta, GA 30322

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14. ABSTRACT Incontinence is a common concern among individuals with autism spectrum disorder. Existing treatments have generally utilized lengthy and invasive procedures and/or lacked methodological rigor. Furthermore, no treatment approach has incorporated medical approaches to address constipation, which is a significant contributor to encopresis in this population. In response to the absence of treatments for this problem, we designed a 2-week multidisciplinary intervention for encopresis (MIE) that combines medical and behavioral approaches. In MIE, gastroenterologist assesses for and treats constipation. Patients also receive outpatient behavioral treatments that include structured sitting on a toilet to promote independent bowel movements. If one does not occur, the behavioral clinician administers a suppository and prompts the child to remain on the toilet. In doing so, continent bowel movements are predictably evoked, allowing for reinforcement. Eventually, the suppositories are gradually faded out to promote independence. The purpose of this study is to demonstrate the efficacy of MIE in a randomized controlled trial with 150 children with ASD. Eligible participants will be randomized to receive two weeks of MIE prior to caregiver training, 1 week of MIE prior to caregiver training, or treatment as usual (TAU).					
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1. INTRODUCTION:

Encopresis is a common concern among individuals with autism spectrum disorder. Existing treatments have generally utilized lengthy and invasive procedures and/or lacked methodological rigor. Furthermore, no treatment approach has incorporated medical approaches to address constipation, which is a significant contributor to encopresis in this population. In response to the absence of treatments for this problem, we designed a 2-week multidisciplinary intervention for encopresis (MIE) that combines medical and behavioral approaches. In MIE, gastroenterologist assesses for and treats constipation. Patients also receive outpatient behavioral treatments that include structured sitting on a toilet to promote independent bowel movements. If one does not occur, the behavioral clinician administers a suppository and prompts the child to remain on the toilet. In doing so, continent bowel movements are predictably evoked, allowing for reinforcement. Eventually, the suppositories are gradually faded out to promote independence. The purpose of this study is to demonstrate the efficacy of MIE in a randomized controlled trial with 150 children with ASD. Eligible participants will be randomized to receive two weeks of MIE prior to caregiver training, 1 week of MIE prior to caregiver training, or treatment as usual (TAU).

KEYWORDS:

Autism Spectrum Disorder, Encopresis, Toileting, Clinical Trial

2. OVERALL PROJECT SUMMARY:

The following Major Tasks were completed in this first year of the project:

- Completed IRB application
- Finalized consent form & human subject protocol
- Completed regulatory documents (regulatory binder)
- Registered study on clinicaltrials.gov
- Trained Independent Evaluators on Parent Target Problem and CGI
- Trained Dr. Muething on Treatment as Usual
- Trained Research Assistant on MIE (1 and 2 week)
- Purchased child materials (toys, stickers, etc.)
- Developed recruitment materials
- Completed database
- Trained Research Coordinators on data entry system
- Began Enrollment & Randomized first participant
- Convened first DSMB meeting
- Enrolled 22 total participants

Changes

Over the past year, the protocol has had four revisions, which documented the following changes:

Protocol Version 3.5 (drafted 11/27/2017)

- Added caregiver log of frequency of child's continent and incontinent bowel movements to the time period between the phone screen and characterization appointment

- Added the Mullen Scales of Early Learning (MSEL) as a possible cognitive measure for participant characterization
- Added research coordinators to the list of personnel who can administer characterization measures
- Renamed enrollment activities using the terms “Characterization” and “Medical Evaluation” to differentiate these activities from Phone Screen
- Stipulated that the Characterization and Medical Evaluation can take place across 1 or 2 days
- Corrected an error in the dosing of the suppository
- Increased the visit windows for Endpoint and Follow up
- Added Midpoint to the schedule of measures
- Added statement that the BPI will be reviewed by a doctoral level member of the study team at Characterization to determine whether potential participants meet exclusion criterion due to interfering problem behavior
- Clarified that the sequence of Characterization and Medical Screening can vary
- Clarified that the TAU appointment can last up to 2 hours, but does not have to last exactly 2 hours
- Added a section describing the informed consent process
- Added the Verbal Consent form to the Screening process

Protocol Version 3.5 (drafted 01/08/2018)

- Specified that randomization to group assignment will now take place after Characterization and Medical Screening are completed (after all eligibility criteria have been met)
- Clarified that visit windows for Week 4 (midpoint), Week 8 (endpoint), and Week 28 (follow-up) will be counted from Baseline Visit (the day baseline measures are collected)
- Added concomitant medication log to table of measures, Baseline, Midpoint, Endpoint and Follow-up

Protocol Version 3.6 (drafted 3/1/2018)

- Edited the protocol to state that we will now be using the Oral Consent and HIPAA Authorization Script and Information Sheet For Research Study Screening instead of the Screening Protocol

Protocol Version 3.7 (drafted 06/18/2018)

- Revised the Medical Screening procedure to allow it to be conducted by a nurse practitioner following training by and with consultation from a pediatric gastroenterologist. This change was initiated to allow for an increased rate of enrollment and to conduct enrollment during times when Dr. McElhanon is unavailable.
- Specified that participants will no longer be enrolled in IRB #53959, which was instituted center-wide at the study site (i.e., Marcus Autism Center) and gave caregivers the opportunity to consent to adding their name to a recruitment registry. If they consented, investigators for other studies could contact them to see if they were interested in participating in those other studies for which they may have been eligible. After some in depth conversations with the Emory IRB, IRB #53959 was discontinued center-wide, so it was removed from our protocol as well.

In addition, we requested a waiver of assent (drafted 2/28/2018)

After enrolling the first few participants we recognized the possibility of participants actively refusing to assent to participation. Specifically, in our pilot study and while conducting a similar

treatment protocol within our clinic, the vast majority of the participants/patients were unable to provide assent because of their age (<6 years old) or cognitive level (e.g., completely nonverbal). However, in anticipation of the possibility that in this much larger study there was a possibility of encountering a potential participant capable of providing assent, we proactively requested a waiver of assent. Our rationale for requesting a waiver of assent was based on a) the fact that the condition being treated in this study is refusal to participate in toileting routines. Thus, one could consider active refusal to be the target of the intervention; and b) the high potential for there to be significant benefit resulting from participation that outweighs the potential impact on self-determination/autonomy. The Emory University IRB granted a waiver of assent on 3/15/18.

Personnel

The study team has largely remained unchanged since start-up. The Principal Investigator, Co-Investigators, and Data Analytics Team have not changed. However, a few changes have occurred in the personnel performing the roles of Data Coordinator, Research Coordinator, and Clinician:

Prior to commencement of the study Dr. Colin Muething transitioned from a Post-Doctoral Fellow and joined the faculty at Emory University. His role on the study did not change, as he is the Clinician primarily responsible for delivery of the Treatment As Usual intervention for participants randomized to that arm. However, with an increased salary, it was necessary to decrease his effort on the study slightly.

In February 2018, Data Coordinator Katie Wilcox left Marcus Autism Center. Jonathan Park assumed Data Coordinator responsibilities immediately upon her departure. Prior to this Jonathan had been performing these responsibilities for other studies at Marcus Autism Center for several years, including submission of data to NDAR, a task he successfully performed for this study this year after assuming the Data Coordinator role.

In July 2018, Shannon Hewett, who had been performing the duties of primary Research Coordinator left Marcus Autism Center. Ansley Reich, who had been assisting with these responsibilities, took over the primary role of Research Coordinator at that time.

Problems

To meet the ambitious recruitment goals specified in the protocol and requested by reviewers, we began enrolling participants on 10/25/2017 after receiving approval from the Emory University IRB. At the time, we were not aware that we needed additional approval from HRPO. When we were informed of this oversight on 2/27/18, we immediately discontinued all recruitment efforts. HRPO approved our protocol and authorized re-initiation of recruitment on 4/10/18. We note that restarting recruitment requires time to get the word out to caregivers, parent support groups, and area clinicians. Potential participants have to be screened and guided through the two-week pre-treatment baseline. Thus, we did not enroll another participant until 5/2/18. This eight-week delay resulted in a substantial setback in our recruitment efforts and we are below our enrollment target of 32 participants in this first year of the study.

Our original enrollment goal was to screen 3-4 children per month. We are pleased to report that in the period since recruitment was put on hold we have met that expectation. However, to catch up with participant accrual that fell behind during that time, we have undertaken efforts to begin scheduling two screening visits per week. This plan will require additional coverage from a medical provider to conduct medical screenings. On 6/18/18, we submitted an amendment to the

Emory University IRB to add a Pediatric Nurse Practitioner (Monica Hannah, PNP) with expertise in ASD to conduct these medical screenings. The PNP will work in close collaboration with the study Pediatric Gastroenterologist (Dr. Barbara McElhanon; see “Changes” above). This amendment was approved by Emory IRB on August 27th, 2018. The next day we submitted this proposed change to HRPO for review, and received approval last week (9/26/18).

We have obtained a partial HIPAA waiver that allows us to identify potential participants from the electronic medical record who have undergone treatment for enuresis at the Marcus Autism Center. This plan is integral to our recruitment efforts because our inclusion criteria require children to be continent for urinations, but incontinent for bowel movements. Data from our clinic indicate that approximately 50% of children with ASD who complete treatment for enuresis remain incontinent for bowel movements six months later, making them very likely to meet eligibility criteria for this study. Given the throughput of patients for this clinical service, this source of potential participants would have been adequate to meet our original enrollment targets of approximately one enrollment visit/week.

However, with our current plans to increase enrollment efforts to allow up to two enrollment visits/week, we have deemed it important to increase our pool of potential participants. To this end we have also reached out to a variety of sources for referrals in metro Atlanta. For example, we have contacted the clinical team who conduct toilet training for enuresis at Emory Autism Center, as well as pediatric gastroenterology practices, psychologists who specialize in diagnostic evaluations for ASD, special education departments who oversee educational services for children with ASD and Board Certified Behavior Analysts who provide ABA services to children with ASD. We have also posted IRB-approved flyers to email listservs for parents of children with ASD and on the Marcus Autism Center Facebook page. These efforts have resulted in additional referrals. Over the next few months we will evaluate the success of these enrollment strategies. We anticipate that we will be able to recover from the suspension of recruitment efforts experienced earlier this year and achieve our recruitment target for the second year of this project.

Participants

To date, we have screened 60 potential participants for this study. Of those, the parents of 24 children have consented to enroll the child into the study (40.0%). Only one participant who attended the in person screening failed to meet inclusion criteria, indicating that our screening process is effectively identifying potential participants who are interested and likely to meet inclusion criteria. In addition, one potentially eligible participant declined to enroll in the study.

Total rate of attrition is currently 12.5% (3 of 24 enrolled participants). Attrition for two of these three participants can be attributed to our early enrollment process. That is, at the time the study commenced caregivers of potentially eligible participants were asked during Phone Screening to record two weeks of data on their child’s bowel movements to aid in determining whether they met inclusion criteria. However, very few caregivers collected adequate data as requested. As a result, two participants were enrolled and randomized prior to determination that they did not meet inclusion criteria during Baseline data collection because they did not meet the definition of encopresis employed in this study. As a result, we altered our enrollment procedure such that any caregiver who did not have adequate data collected to rule out exclusion for this reason at the time of enrollment would be consented and undergo characterization, but randomization is postponed until after Baseline data collection confirm that they meet all inclusion criteria. We have not had to drop any participants after making this change. We expect to maintain this much lower rate of attrition for the remainder of the study.

3. KEY RESEARCH ACCOMPLISHMENTS:

Nothing to report

4. CONCLUSION:

Although study startup initially went well, including training of the study team, developing study procedures, obtaining IRB approval, and establishing the data base, suspension of recruitment while awaiting HRPO approval prevented us from meeting original recruitment targets. Despite this setback, we have set in place several strategies to increase the rate of subject accrual in order to catch up with recruitment by the end of Year 2.

5. PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:

(1) Lay Press: None

(2) Peer-Reviewed Scientific Journals: None

(3) Invited Articles: None

(4) Abstracts: None

- a. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.

Nothing to report

6. INVENTIONS, PATENTS AND LICENSES:

Nothing to report

7. REPORTABLE OUTCOMES:

Nothing to report

8. OTHER ACHIEVEMENTS:

Nothing to report

9. REFERENCES:

Nothing to report

10. APPENDICES:

Nothing to Report

TRAINING OR FELLOWSHIP AWARDS:

Several undergraduate practicum students participated in this project, including Jamila Pitts, Melanie Parks, Jazmin Simms, Jordyn Smith, and Mary Elmore Demott. These students assisted in conducting the Multidisciplinary Intervention for Encopresis treatment protocol, collected and graphed data, made recruitment calls, and assisted with administrative work (e.g., preparing for client consent and characterization visits, filing, creating participant folders, etc.).

COLLABORATIVE AWARDS:

Nothing to Report

MARKING OF PROPRIETARY INFORMATION:

Nothing to Report